Obstructive sleep apnea: neurocognitive and behavioral functions before and after treatment

Katherine Turner[a]
Elena Zambrelli[a]
Sara Lavolpe[a]
Cristina Baldi[a]
Francesca Furia[a]
Maria Paola Canevini[a,b]

[a] Sleep Medicine-Epilepsy Center, ASST Santi Paolo e Carlo, San Paolo Hospital, Milan, Italy
[b] Department of Health Sciences, University of Milan, Italy

Correspondence to: Katherine Turner
E-mail: katherine.turner@asst-santipaolocarlo.it

Summary

Obstructive sleep apnea syndrome (OSAS) is a sleep disorder characterized by repetitive episodes of upper airway obstruction. The aim of this study was to evaluate whether continuous positive airway pressure (CPAP) treatment is linked to improvements in cognitive abilities and emotional functions of patients with OSAS.
Following the exclusion of four subjects for non-adherence to CPAP treatment, the final study sample was composed of 16 patients with moderate-to-severe OSAS, who were assessed both prior to and after 3 months of CPAP treatment, using a neuropsychological battery and questionnaires to assess mood and anxiety disorders, irritability, quality of life, quality of sleep and daytime sleepiness.
We observed significant improvements in Digit Span Backward, Short Story and Corsi Span performances after 3 months of CPAP treatment. Questionnaires showed a significant reduction in daytime sleepiness and improvements in the subjective perception of sleep quality and sleep efficiency, and reduced daytime dysfunction.
CPAP treatment has significant effects on different cognitive domains in patients with OSAS, especially working memory, long-term verbal memory, and short-term visuospatial memory.

KEY WORDS: continuous positive airway pressure (CPAP), memory, obstructive sleep apnea syndrome (OSAS).

Introduction

Obstructive sleep apnea syndrome (OSAS) is a sleep disorder characterized by repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction occurring during sleep. These events often result in reductions in blood oxygen saturation and are usually terminated by brief arousals from sleep. By definition, apneic and hypopneic events last a minimum of 10 seconds (American Academy of Sleep Medicine, 2014). A constant feature of OSAS is snoring, which leads to sleep fragmentation. Excessive sleepiness is a major presenting complaint in many but not all cases. Sleepiness in OSAS is most evident in relaxing or inactive situations.
OSAS is a frequently under-recognized condition. The prevalence of this syndrome varies between 9% and 15% of adults between the fifth and the seventh decades of life, and it is more frequent in males (Ferini-Strambi et al., 2004). Most studies estimate the prevalence of OSAS to be about 3 to 7% in men and 2 to 5% in women, although the rate varies in subpopulations with certain comorbidities and across different regions (Bixler et al., 2001).
Patients with OSAS, suffering from long-term cardiovascular and cerebrovascular symptoms, are more exposed to cardiovascular pathology such as hypertension or stroke, with a probability approximately four times higher than the general population (Yaggi et al., 2005).
OSAS alters the functional and structural characteristics of large arteries, contributing to the onset and evolution of atherosclerosis (Macey et al., 2002).
Obesity, particularly upper body obesity, is common in OSAS, and there is evidence that patients with the syndrome are particularly prone to have enlarged necks. Neck circumference is a strong predictor of OSAS. Values less than 37 cm and greater than 48 cm are associated with low and high risk, respectively.
Another long-term effect of OSAS is a decrease in gray matter in the hippocampus, anterior cingulate cortex, ventrolateral frontal cortex, and a portion of the cerebellar cortex. Devita et al. reported morphological changes, such as brain tissue damage, associated with impairment of cognitive functions, including attention, executive functioning, motor efficiency, working memory and long-term episodic memory, in patients with OSAS (Devita et al., 2017).
Some Authors have found that the lack of restful sleep affects quality of life in these patients, the most prominent symptom being excessive daytime sleepiness (Mu et al., 2017).
There is also some clinical evidence of a correlation between OSAS and the risk of developing aggressive behavior, depressive disorders and anxiety symptomatology (Acheson et al., 2007).
The first-line treatment of choice for OSAS is continuous positive airway pressure (CPAP) treatment, which re-establishes normal levels of nocturnal oxygenation (Patil et al., 2019). Sleep fragmentation, oxyhemoglobin desaturation, excessive daytime sleepiness and cognitive functions usually improve after the start of CPAP treatment (Devita et al., 2018).

The main objective of the present study was to evaluate, after three months of CPAP treatment, the reversibility of cognitive impairments potentially attributable to OSAS. This is a single-center, add-on, open study: patients with OSAS were assessed both before CPAP treatment (baseline, T0) and after 3 months (T3) of CPAP use. A further aim was to investigate potential effects of the treatment on mood, quality of life and sleep in those who suffer from this disorder.

Materials and methods

We enrolled, at the Sleep Medicine-Epilepsy Center, San Paolo Hospital, University of Milan, 20 patients (15 men and 5 women) aged between 34 and 80 years and affected by moderate-to-severe OSAS. The inclusion criteria were: a diagnosis of OSAS made according to the criteria of the International Classification of Sleep Disorders-Third Edition (American Academy of Sleep Medicine, 2014), an age of 18 years or over, at least 8 years of education, and the ability to speak, understand and read Italian.
The following exclusion criteria were applied: presence of previous head trauma, previous encephalitis, intellectual disability (Raven's Coloured Progressive Matrices score < 17.5), claustrophobia and drug or alcohol abuse.
All patients and controls gave their written informed consent prior to completing the questionnaires and undergoing the neuropsychological evaluations.
The protocol was carried out in accordance with the ethical standards of the Declaration of Helsinki, and the San Paolo Hospital ethics committee reviewed and approved the study protocol.
Patients underwent out-of-center sleep testing (OCST) both before treatment and after three months of CPAP treatment. This ventilation treatment started on average 20 days after the baseline OCST.

OCST

OCST devices generally have at least 8 recording channels, which usually include oronasal airflow, chest wall and abdominal effort, body position, snoring and oxyhemoglobin saturation.
In particular, the following indices were obtained:
- Respiratory event index (REI): the number of pathological respiratory events per hour of sleep;
- Supine REI: the number of pathological respiratory events per hour of sleep, in a supine position;
- Non-supine REI: the number of pathological respiratory events per hour of sleep, not in a supine position;
- Oxygen desaturation index (ODI): the number of oxygen desaturations at least 4% below the baseline level per hour of sleep.

CPAP

CPAP titration, aimed at abolishing all apneic events, hypopneic events, and snoring, was performed with the automatic positive airway pressure device in auto-adjustment mode for a period, after which it was switched to a fixed pressure (90th or 95th percentile). OCST proper was performed at the end of each titration period.

Cognitive assessment

The neuropsychological assessment of patients with OSAS consisted of a complete evaluation of the main cognitive functions, namely non-verbal intelligence, memory (verbal and visuospatial, working, short-term and long-term), attention and visuoconstructive functions. The tests used in the assessment are all standardized for the Italian population. The cognitive domains were investigated using the psychometric instruments outlined below.

Non-verbal intelligence
The Raven's Coloured Progressive Matrices is a set of 3 subtests (A, Ab, and B) aimed at evaluating non-verbal intelligence, visual processing speed, cognitive speed and flexibility. Subjects are required to choose from a set of 5 distractors the item logically missing in a given visual/spatial set (Basso et al., 1987).

Memory
Short-term verbal memory and working memory
Forward and backward Digit Span: subjects are asked to listen to and repeat sequences of single digits, both forwards and backwards; the number of digits in each sequence is gradually increased (Monaco et al., 2013).

Short-term visuospatial memory
Corsi Span: 9 identical wooden blocks are arranged in a random order, numbered on the side facing the examiner. The experimenter touches the cubes in a standard sequence of increasing length and subjects are asked to reproduce it by touching the cubes in the same order (Monaco et al., 2013).

Long-term verbal memory
Short Story Test: a short story is read to the subject with the instruction to repeat, immediately afterwards, everything they remember; then, the story is read again. After 10 minutes, the patient is asked to repeat the story once again (Novelli et al., 1986).

Long-term visuospatial memory
Rey-Osterrieth Complex Figure (ROCF), recall/Modified Taylor Complex Figure, recall: the participant is first asked to copy the ROCF as accurately as possible; then, after 15 minutes of verbal activity, he/she is instructed to reproduce the figure from memory without forewarning (Caffarra et al., 2002). The test was repeated after the 3 months of CPAP treatment, but this time (in order to avoid the effect of implicit learning) the Modified Taylor Complex Figure was used instead (Casarotti et al., 2014).

Attention
Attentional Matrices: this test involves the use of rows of numbers randomly interspersed with a designated target number or numbers; the patient is instructed to cross out all target numbers in three matrices («5» in I, «2-6» in II, «1-4-9» in III), arranged in a random sequence, within a time limit of 45 seconds (Spinnler and Tognoni, 1987).

Visuoconstructive functions
In the ROCF, copy and Modified Taylor Complex Figure, copy tasks, the subject is asked to copy a bidimensional complex figure (Caffarra et al., 2002; Casarotti et al., 2014).

Behavioral assessment

Depression

The Beck Depression Inventory-II (BDI-II) is a self-report questionnaire for assessing the severity of depression. It is composed of 21 items, divided into two scales: Somatic-Affective (loss of interest, loss of energy, changes in sleep and appetite, agitation and crying) and Cognitive (pessimism, guilt and self-criticism) (Beck et al., 2006).

Anxiety

The State-Trait Anxiety Inventory (STAI) is a questionnaire for evaluating anxiety disorders. Items are grouped into two separate scales measuring state and trait anxiety; these scales refer, respectively, to how subjects generally feel and what they feel in particular situations (Spielberger et al., 1983).

Aggressive behaviors

The Aggression Questionnaire (AQ) is a self-report questionnaire for assessing an individual's level of aggressiveness/irritability. The following dimensions are evaluated: physical aggression, verbal aggression, anger and hostility (Buss and Perry, 1992; Maffei, 2007).

Quality of life

The SF-12 questionnaire: this is the abridged version of the SF-36 questionnaire, and it allows the investigation of two synthetic indices: PCS (Physical Component Summary) referring to the individual's physical state and MCS (Mental Component Summary) referring to their mental state (Ware et al., 1996).

Sleep

Pittsburgh Sleep Quality Index (PSQI): this is a self-report questionnaire for sleep quality assessment. Patients are asked to answer questions about their sleep behavior over the last month. The questionnaire consists of 7 components: component 1: subjective perception of sleep quality, component 2: sleep latency, component 3: sleep duration, component 4: sleep efficiency, component 5: sleep disturbance, component 6: use of drugs to fall asleep, and component 7: daytime dysfunction caused by sleepiness.

A total score > 5 is indicative of inadequate sleep quality (Buysse et al., 1989). This scale has been validated in the Italian population (Curcio et al., 2013).

The Epworth Sleepiness Scale (ESS) is a self-report scale, used to evaluate subjects' perception of their level of daytime sleepiness. A score >10 is indicative of high levels of daytime sleepiness. This instrument has been validated in the Italian population (Vignatelli et al., 2003).

Sleep/Wake Activity Inventory (SWAI): this is a multidimensional self-assessment scale for the evaluation of daytime sleepiness and subjective sleep disorders. It includes 12 items divided into two parts: Excessive Daytime Sleepiness - EDS (9 items), which provides information about drowsiness, and Nocturnal Sleep - NS (3 items), which is designed to evaluate nighttime sleep (Rosenthal et al., 1993).

Statistical analyses

We used an electronic database and analyzed the data with SPSS 24.0 for Windows.

Continuous variables were presented as mean values and standard deviation (SD).

Student's T-test for independent samples was used to compare neuropsychological scores (pre *vs* post- treatment, and between men and women).

Categorical and ordinal variables were compared using the Mann-Whitney U test where appropriate; continuous variables were compared using Student's t-test after applying Levene's test for equality of variance. If the variance was unequal, nonparametric tests were performed. Simultaneous logistic regression models were used to evaluate the ability of independent variables to predict outcomes. We compared mean scores at T0 and T3 and between genders.

We did not perform a group size calculation; the group sizes in this study were based on the recruitment capacity of our center. The modest sizes of the groups could have increased the risk of false negative findings. The limit of significance (p) was equal or inferior to 0.05 and Cohen's d was calculated as the effect size index.

Results

Twenty patients between 34 and 80 years of age were initially enrolled in the present study. A neuropsychological battery was administered to 16 patients with OSAS before and after CPAP therapy (12 men and 4 women, mean age 53±11 years). The other four subjects (mean age: 69±18 years) were excluded due to problems of CPAP device non-adherence: two of these four patients underwent a second evaluation at T3 and two refused to repeat cognitive assessment after 3 months.

Of the initial 20 patients, three subjects had epilepsy (symptomatic focal epilepsy, cryptogenic focal epilepsy and idiopathic focal epilepsy).

OCST

Statistically significant differences after 3 months of CPAP therapy were found in the REI ($p<0.001$), supine REI ($p<0.001$), non-supine REI ($p<0.001$) and ODI ($p<0.001$).

With regard to gender, no significant differences were observed between men and women at T3 ($p>0.05$).

Cognitive assessment

We found statistically significant improvements in cognitive functioning, i.e. working memory (Digit Span Backward, p=0.004), long-term verbal memory (Short Story Test, p=0.004), and short-term visuospatial memory (Corsi Span, p=0.02) after 3 months of CPAP therapy. The data are summarized in Table I.

No significant changes were observed in the Digit Span Forward (p=0.61), Attentional Matrices (p=0.55), or ROCF/Modified Taylor Complex Figure (copy: p=0.80; recall: p=0.48) performances.

Concerning gender, statistically significant differences emerged in Digit Span Backward (p=0.04) and ROCF/Modified Taylor Complex Figure, recall (p=0.03) performances, with the men outperforming the women (Table II).

Behavioral assessment

No statistically significant improvements were found in the BDI-II, STAI, AQ or SF-12 questionnaire scores after 3 months of treatment (Table I).

Table I - Neuropsychological tests and questionnaires assessed at T0 and T3.

	T0 (n=16)		T3 (n=16)		T-test	p value
	Mean	SD	Mean	SD		
REI	**30.92**	**11.21**	**3.85**	**4.06**	**t(14.71)=8.25**	**<0.001**
Supine REI	**45.73**	**22.29**	**8.67**	**9.26**	**t(14.68)=5.32**	**<0.001**
Non-supine REI	**25.16**	**13.16**	**2.42**	**3.95**	**t(11.65)=5.51**	**<0.001**
ODI	**28.43**	**11.78**	**4.95**	**5.43**	**t(18.02)=6.81**	**<0.001**
Digit Span Forward	5.62	1.02	5.81	1.05	t(30)=-0.5	0.61
Digit Span Backward	4.13	0.7	5.12	1.02	t(29)=-3.01	0.004
Corsi Span	**4.94**	**0.9**	**5.6**	**0.6**	**t(30)=-2.46**	**0.02**
Short Story Test	**10.19**	**3.72**	**13.84**	**2.89**	**t(30)=-3.1**	**0.004**
ROCF/ Taylor, recall	19.08	7.32	21.09	7.69	t(27)=-0.72	0.48
Attentional Matrices	54.0	6.0	55.06	3.85	t(30)=-0.6	0.55
ROCF/Taylor, copy	34.46	2.10	34.25	2.43	t(27)=0.25	0.80
BDI-II	11.27	8.68	7.27	8.0	t(28)=1.31	0.20
STAI	42.80	11.36	38	13.23	t(28)=1.07	0.30
AQ	58.13	14.1	56.87	16.25	t(28)=0.23	0.82
SF-12	31.27	2.91	31.20	2.76	t(28)=0.06	0.95
PSQI component 1	**1.81**	**1.0**	**0.81**	**0.65**	**t(30)=3.24**	**0.003**
PSQI component 2	1.06	0.77	0.75	0.77	t(30)=1.14	0.26
PSQI component 3	1.75	1.06	1.31	1.01	t(30)=1.19	0.24
PSQI component 4	1.56	1.26	0.69	1.19	t(30)=2.01	0.05
PSQI component 5	1.56	0.89	1.13	0.61	t(30)=1.61	0.12
PSQI component 6	0.69	1.14	0.5	1.03	t(30)=0.49	0.63
PSQI component 7	**1.19**	**1.17**	**0.44**	**0.63**	**t(23.04)=2.26**	**0.03**
PSQI Total	**7.75**	**5.27**	**5.56**	**3.61**	**t(30)=1.37**	**0.18**
ESS	**9.31**	**5.87**	**5.69**	**3.44**	**t(24.2)=2.13**	**0.04**
SWAI	35.31	9.96	38.16	5.56	t(30)=-1	0.33

Abbreviations: REI: respiratory event index; ODI: oxygen desaturation index; ROCF: Rey-Osterrieth Complex Figure; Taylor: Modified Taylor Complex Figure; AQ: Aggression Questionnaire; BDI-II: Beck Depression Inventory; STAI: State Trait Anxiety Inventory; PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale; SWAI: Sleep/Wake Activity Inventory.

No significant differences between men and women were found in the scores on any of the self-administered questionnaires (Table II).

Sleep

We observed a significant improvement after 3 months in the average scores for PSQI components 1, 4 and 7, which evaluate, respectively, the subjective perception of sleep quality (T0=Mean: 1.81, SD: 1.0; T3=Mean: 0.81, SD: 0.65, p=0.003), sleep efficiency (T0=Mean: 1.56, SD: 1.26; T3=Mean: 0.69, SD: 1.19, p=0.05), and daytime dysfunction caused by sleepiness (T0=Mean: 1.19, SD: 1.17; T3=Mean: 0.44, SD: 0.63, p=0.03).

Significant differences were also found in the ESS scores after CPAP treatment (T0= Mean: 9.31, SD: 5.87; T3=Mean: 5.69, SD: 3.44, p=0.04).

There were no significant differences in the SWAI scale scores.

With regard to gender, no significant differences in sleep questionnaire performances were observed between men and women, either at T0 or T3.

Scores of patients not receiving CPAP treatment

The scores of subjects who did not receive CPAP due to device non-adherence, were also analyzed: these subjects showed no significant improvements in neuropsychological test or questionnaire scores at T3.

Scores of patients with epilepsy

Out of three subjects with epilepsy, one did not use CPAP. In the other two, no significant improvements in the cognitive and psychological test scores were observed.

Discussion

The subjects with OSAS investigated in the present study showed a high variability in their neuropsychological profiles, as shown by the range of raw scores obtained. However, comparison of T0 and T3 performances revealed statistically significant improvements in working memory, long-term verbal memory and short-term visuospatial memory after use of CPAP. Our results are consistent with those of previous studies, in which CPAP treatment was correlated with better performances, especially with regard to memory and executive functions (Ferini-Strambi et al., 2003).

Table II - Neuropsychological test and questionnaires of men *vs.* women assessed at T3.

	Men (n=12)		Women (n=4)		T-test	p value
	Mean	SD	Mean	SD		
REI	3.41	3.83	5.07	5.02	t(4.34)=0.6	0.5
Supine REI	9.64	10.26	6.75	7.83	t(7.88)=0.54	0.6
Non-supine REI	2	2.58	3.27	6.35	t(3.5)=-0.38	0.72
ODI	4.28	4.91	6.8	7.17	t(4.07)=-0.65	0.55
Digit Span Forward	**5.77**	**0.93**	**5.2**	**1.09**	**t(16)=1.03**	**0.28**
Digit Span Backward	4.33	0.65	3.6	0.55	t(15)=2.2	0.04
Corsi Span	5.08	0.95	4.4	0.55	t(16)=1.88	0.16
Short Story Test	9.92	2.98	12	5.27	t(16)=-1.12	0.28
ROCF/ Taylor, recall	**20.04**	**6.78**	**10**	**5.29**	**t(13)=2.37**	**0.03**
Attentional Matrices	53.92	6.51	53.4	5.18	t(16)=0.16	0.87
ROCF/Taylor, copy	34.5	2.19	31.67	5.86	t(2.14)=0.82	0.49
BDI-II	9.75	9.08	13.8	6.42	t(15)=-0.9	0.38
STAI	41.67	12.49	43.8	5.17	t(15)=-0.36	0.72
AQ	52.75	14.64	60.8	11.32	t(15)=-0.41	0.68
SF-12	31.42	3.09	30.8	3.35	t(15)=0.37	0.72
PSQI component 1	1.69	0.95	2	1.22	t(16)=-0.57	0.58
PSQI component 2	**1.31**	**0.75**	**0.6**	**0.55**	**t(10.11)=1.9**	**0.07**
PSQI component 3	1.77	0.83	1.8	1.64	t(4.81)=-0.04	0.97
PSQI component 4	1.46	1.2	1.8	1.64	t(16)=-0.49	0.63
PSQI component 5	1.62	0.87	1.4	0.89	t(16)=0.47	0.65
PSQI component 6	0.69	1.18	1	1.41	t(16)=-0.47	0.64
PSQI component 7	1.0	1.15	1.2	1.3	t(16)=-0.32	0.75
PSQI Total	7.69	5.3	8.6	4.56	t(16)=-0.34	0.73
ESS	8.85	5.79	10.0	6.4	t(16)=-0.37	0.71
SWAI	37.0	10.7	33.8	6.56	t(16)=0.62	0.54

Abbreviations: REI: respiratory event index; ODI: oxygen desaturation index; ROCF: Rey-Osterrieth Complex Figure; Taylor: Modified Taylor Complex Figure; AQ: Aggression Questionnaire; BDI-II: Beck Depression Inventory; STAI: State Trait Anxiety Inventory; PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale; SWAI: Sleep/Wake Activity Inventory.

Obstructive sleep apnea syndrome has significant implications for cognitive functioning, as pointed out by some Authors, who have shown it to be associated with worse performances on tests of memory, sustained attention, executive functions, and visuoconstructive abilities (Ferini-Strambi et al., 2003). However, the cause of these impairments is still under debate: some authors reported that cognitive decline in OSAS is linked exclusively to daytime sleepiness, which is a result of the fragmentation of sleep caused by frequent sleep apneic events (Cheshire et al., 1992); others have linked it to nocturnal hypoxia (Findley et al., 1986). Recent studies, however, propose that both daytime somnolence and nocturnal hypoxia may contribute to cognitive impairments in patients with OSAS: in particular, it has been suggested that deficits in executive functions and in motor and visuoconstructive abilities may be related to the severity of hypoxia, while performance in memory and attention tasks could be associated with daytime sleepiness (Doran et al., 2001).

Several Authors have identified predictors of improvements in neuropsychological functioning observed in patients using CPAP: Kingshott et al. (2000) reported that improvements may be related to the severity of apnea at baseline (i.e. before treatment); conversely, they found the frequency of nocturnal arousals and the apnea-hypopnea index at baseline to be poor predictors of the outcome of CPAP treatment (Bennett et al., 1998).

The severity of OSAS can be predictive of improvements in clinical symptoms, quality of life, and post-treatment response, while other authors (Redline et al., 1997) found that sleep fragmentation and the frequency of apnea/hypopnea at baseline can reliably predict improvements in daytime sleepiness.

Our data demonstrated a statistically significant improvement in working memory after CPAP treatment, in accordance with other studies. On the contrary, in patients who did not use CPAP for three months, scores on Digit Span Backward did not change (Naëgelé et al., 1998).

Some Authors maintain that cognitive deficits in patients with OSAS are associated with structural changes in the brain, such as volume reductions of gray matter in the left hippocampus, the left posterior parietal cortex, and the right upper frontal gyrus. Clinical improvements observed following CPAP treatment have been correlated with an increase in the volume of gray matter in the hippocampus, suggesting that cognitive and structural deficits in OSAS are secondary to sleep deprivation and to repeated nocturnal hypoxia episodes, and that they can therefore be restored through an adequate treatment, thanks also to hippocampal plasticity (Canessa et al., 2011).

Another interesting result from our work concerns the im-

provement seen in long-term verbal memory performance (Short Story Test), which is in line with the findings of Zimmerman et al. (2006), who, albeit using a different tool (Hopkins Verbal Learning Test-revised) to evaluate memory functions, found significant improvements after three months of CPAP treatment.

Whereas we observed a statistically significant improvement in short-term visuospatial memory evaluated with the Corsi Span, some studies have not shown significant differences after treatment with CPAP (Naëgelé et al., 1998). Instead, the work of Canessa et al. (2011) is in line with our results.

Concerning the impairment of short-term verbal memory and its potential reversibility, the literature offers conflicting views. While some Authors showed worse short-term verbal memory performances in patients compared with the control group (Borak et al., 1996), others did not observe significant differences (Feuerstein et al., 1997).

Another cognitive domain explored was attention: in this regard, a clear, albeit not statistically significant, difference was observed (T0 Mean: 54.0, SD: 6.0; T3 Mean: 55.06, SD: 3.85). This failure to reach statistical significance could be explained by the fact that the participants already recorded high scores, even before the treatment. Ferini-Strambi et al. (2003) also reported no significant improvements in this function; in this case, the performance of the patients compared to the control group was under the normal range before treatment. However, attention is a multidimensional cognitive function, within which it is possible to identify two main dimensions: intensity and selectivity. The first consists of two components: alert/vigilance and sustained attention. The selectivity dimension consists of two other components: selective attention and divided attention (van Zomeren and Brouwer, 1994). The Attentional Matrices evaluate selective attention, and in the present work no significant improvements were observed in this dimension.

We also evaluated emotional outcomes, behavioral outcomes and quality of life in our patients with OSAS receiving CPAP treatment for 3 months: no statistically significant differences in mood, anxiety or aggression were found. In the literature, data on mood disorders vary: some authors (Sanchez et al., 2001) observed significantly lower levels of depressive and anxious symptoms after 3 months of CPAP treatment, leading them to hypothesize that the use of CPAP improves quality of life and reduces depressive symptomatology, while others found no improvement in emotional status (Kawahara et al., 2005). There also emerge clear discrepancies regarding improvement of quality of life: no significant changes were observed in our research, whereas other authors have stressed that patients with good treatment compliance can benefit, obtaining a reduction in symptoms and daytime drowsiness and a better quality of life (Avlonitou et al., 2012). The questionnaire used in our study (SF-12) provides a general profile of quality of life (since it contains areas evaluated with a single item); a more detailed questionnaire, e.g. the SF-36, could have provided a more accurate assessment of quality of life.

From the perspective of gender, the present work showed that the men, after 3 months of CPAP treatment, had significantly better scores on the Digit Span Backward and ROCF/Modified Taylor Complex Figure, recall. In a study conducted by Ye et al. (2009), significant differences were found, before CPAP treatment, between men and women with OSAS (the women had higher levels of daytime sleepiness, resulting in lower functional status, higher frequency of OSAS symptoms, greater deflation of mood, and worse performance on neuropsychological tasks), whereas after CPAP therapy, the men and women showed significant differences in neuropsychological outcomes and in the degree of compliance with treatment.

Finally, we compared cognitive performances of patients with epilepsy vs. patients without epilepsy: we did not identify any statistically significant differences. In the literature a strong comorbidity is reported between sleep disorders and epilepsy, since epilepsy is sensitive to the fragmentation of sleep: apneas, sleep fragmentation and hypoxia can increase cortical excitability and provoke seizures (Manni et al., 2003).

In conclusion, this work shows that CPAP treatment has significant effects on cognitive functioning. Improvements in apnea severity indices and in the O2 desaturation index were observed, but significant improvements also emerged in working memory, long-term verbal memory and short-term visual and spatial memory. With regard to psychological aspects, no significant improvements emerged in performances on the questionnaires used to assess mood, anxiety, aggressive behavior and quality of life, however it must be recalled that these scores were normal before the start of the treatment. The use of CPAP was also associated with significant reductions in daytime sleepiness and daytime dysfunction. When dividing the sample by presence/absence of epilepsy and by gender, no differences were apparent.

The limitations of this study are the heterogeneity of the sample (age and gender) and its small size. Our preliminary results suggest that the occurrence of OSAS in patients with epilepsy deserves further examination and that new studies are necessary to support our findings in this subgroup (i.e. no significant improvements in the cognitive and psychological test scores).

Furthermore, since we did not compare the patients' performances with those of a healthy control group at T0 we were not able to establish the extent to which our group of patients (albeit not presenting pathological scores) performed worse than healthy subjects. Nevertheless, the study highlighted the effectiveness and usefulness of CPAP, which was demonstrated to be a valid tool for the treatment of OSAS symptoms; furthermore, with regard to its effectiveness, it should be emphasized that this treatment impacts not only on the aspects strictly connected with OSAS, but also on cognitive functioning.

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